## REMARKS/ARGUMENTS

Rejection Under 35 USC 102(b)

Claims 1-5 have been rejected under 35 USC 102(b). More specifically, the Patent Office states, "Ried et al. teaches a set of chromosomal probes comprising the combination of two probes 5p and 3q." This rejection has been obviated by the claim amendment set forth above.

Rejections Under 35 USC 103(a)

Claim 6 has been rejected under 103(a) over Halling et al. (U.S. Pat. No. 6,376,188), in view of McGill et al. (U.S. Pat. No. 5,658,730), further in view of Bastian et al. (U.S. Pat. No. 6,465,180). More specifically, the Patent Office states:

> Halling et al. teaches a set of three chromosomal probes comprising the combination of 9p21 locus specific probe and probe of chromosome 8...McGill et al. teaches specifically chromosomal probe 8q24...Bastian et al. teach a 5p15 locus specific probe. It would have been prima facie obvious to one having ordinary skill in the art at the time the invention was made to combine and substitute a method, wherein one of the probes is 5p15 locus specific probe of Bastian et al. into the set of three chromosomal probes of Halling et al., in view of McGill et al...in order to improve the analysis of a plurality of target nucleic acid involved in different diseases.

Applicant respectfully traverses this rejection. While Halling et al. does teach the use of a set of chromosomal probes for detecting cancer, the set comprising a 9p21 probe and a chromosome 8 probe, Halling et al. does not specify the group of probes consisting of 5p15, 8q24, and 9p21. As noted by the Patent Office, McGill et al. teaches the use of an 8q24 probe for detecting prostate cancer, and Bastian et al. teaches the use of a 5p15 probe in a set for detecting melanoma. While each reference discloses a single probe of the combination in Applicant's Claim 6(a), none of the

references disclose the particular **combination** of probes cited in Applicant's Claim 6. Applicant's discovery pertains to the selection of a **particular** combination of probes that identifies cancer with a high diagnostic value. Applicant has provided evidence that not all probes provide the same diagnostic values as a combination as they do alone, or in combination with **any** other probe. The particular combination of 5p15, 8q24, and 9p21 provides a more sensitive indicator of the presence of cancerous tissue than the individual probes disclosed in McGill et al. and Bastian et al. In addition, this particular combination provides a more sensitive indicator than **any** set of three probes comprising 9p21, **any** chromosome 8 probe, and an **unidentified** probe as disclosed in Halling et al.

It would not be prima facie obvious to one of skill in the art to substitute and combine the 8q24 probe of McGill et al. and 5p15 probe of Bastian et al. into a set with the 9p21 probe of Halling et al. One of skill in the art would not be able to predict with any degree of certainty that the **particular** combination of probes would provide a more sensitive and accurate indicator of cancer than each probe individually or in combination with any other probe. One of skill in the art would not have been able to predict with any degree of certainty that the 5p15, 8q24, and 9p21 probes would complement each other in providing enhanced sensitivity and specificity than conventional methods previously known in the art.

Claim 7 has been rejected under 103(a) over Bastian et al. in view of McGill et al., further in view of Vogelstein et al. (U.S. Pat. No. 6,127,126), further in view of Nuell et al (U.S. Pat. No. 5,658,792). More specifically the Patent Office states:

> Bastian et al. teaches a set of chromosomal probes comprising the combination of 5p15 locus specific probe...McGill et al. teaches specifically chromosomal probe 8q24...Vogelstein et al. teach a 7p12 locus specific probe ...Nuell et al. teach a 17q21 locus specific probe...By employing scientific reasoning, an ordinary artisan would have combined and substituted a method, wherein one of the probes is 17q21 locus specific probe of Nuell et al. into the set of chromosomal probes of

> Bastian et al. in view of McGill et al. further in view of McGill et al. further in view of Vogelstein et al in order to improve the analysis of a plurality of target nucleic acid involved in different diseases.

Applicant respectfully traverses this rejection. While Bastian et al. does teach the use of a set of chromosomal probes for detecting cancer, the set comprising a 5p15 probe and a region 6p probe, Bastian et al. does not specify a group of **four** probes including 5p15. In addition, Bastian et al. does not specify which additional probes are necessary for the combinations disclosed in Claim 7. As stated by the Patent Office, McGill et al. teaches the use of an 8q24 probe for detecting prostate cancer, and Bastian et al. teaches the use of a 5p15 probe in a set for detecting melanoma. While each reference discloses a single probe of the combination in Applicant's Claim 7, none of the references disclose the particular **combination** of probes cited in Applicant's Claim 7. Applicant's discovery pertains to the selection of a **particular** combination of probes that identifies cancer with a high diagnostic value. It should be noted that Applicant has provided evidence that not all probes provide the same diagnostic values as a combination as they do alone or in combination with **any** other probe. The particular combinations of probes disclosed in Claim 7 provide more sensitive indicators of the presence of cancerous tissue than the pair of probes disclosed in Bastian et al., as well as the individual probes taught by McGill et al., Vogelstein et al., and Nuell et al.

It would not be prima facie obvious to one of skill in the art to substitute and combine the 8q24 probe of McGill et al., the 7p12 probe of Vogelstein et al., and the 17q21 probe of Nuell et al. into the 5p15 and region 6p pair of probes of Bastian et al. One of skill in the art would not be able to predict with any degree of certainty that the **particular** combinations of probes disclosed in Claim 7 would provide a more sensitive and accurate indicator of cancer than each probe individually or in combination with any other probe. One of skill in the art would not have

been able to predict with any degree of certainty that the combinations of three probes disclosed in Claim 7 would complement each other in providing enhanced sensitivity and specificity than conventional methods previously known in the art.

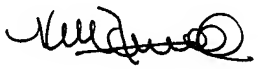
Applicant's results of using combinations of probes are not merely additive in nature. Combining individual probes into a set would not necessarily result in a better diagnostic measure equal in magnitude to the number of probes combined. Certain probes may yield false positives more or less easily than other probes by virtue of their sequence. Signal-to-noise ratios can also vary from probe to probe. Adding a probe to a set could therefore decrease assay specificity. It would not be obvious to one of skill in the art to combine the particular stated probes in order to improve the analysis of a plurality of target nucleic acids involved in a particular disease state. Prior to Applicant's discovery, the identities of the specific combinations of probes that would provide a more sensitive indicator of cancer were unknown. In addition, if only one particular chromosomal aberration were sufficient for an onset of cancer, one of skill in the art would expect that a single probe to that aberration would provide the best indicator of cancer and that assaying additional probes would only decrease assay sensitivity. One of skill in the art would not expect that assaying the same tissue with additional probes in this case would result in a more sensitive and hence better indicator of cancer. If only one particular chromosomal aberration were sufficient for an onset of cancer, one would expect multiple probes to provide a less sensitive indicator in a combinatorial analysis than the single probe case. Aberrations at a second chromosomal locus, however, might only elicit cancer when in combination with other specific aberrations, but when presented alone might not be sufficient to trigger an onset of cancer. In this case, a particular combination of probes would provide a

better indicator of cancer than any of the single probes alone. Prior to applicant's discovery, the distinction was not made, and was therefore not known in the art.

Summary

In light of the above amendment, consideration of the subject patent application is respectfully requested. Any deficiency or overpayment should be charged or credited to Deposit Account No. 500282.

Respectfully submitted,



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